

Remarks

Applicants wish to thank Examiner Meller for conducting an in person interview with Applicant's attorney, Greg Zayia, on May 28, 2003.

By way of the above amendments, Claims 7, 8, 10, and 18-20 remain pending in this application. These amendments serve merely to consolidate the claims. In the Final Office Action, Examiner maintained the rejection of Claims 7-11 and 17-20 under 35 U.S.C. §103 over Braswell in view of Facino and Intellisano. Specifically, Examiner maintained that the foregoing references as a whole teach a method of inducing phase II enzymes in subjects in need thereof comprising administering to the subject a lipid-soluble *Echinacea* extract. This rejection is again respectfully traversed as conceivably applied to the amended claims.

Braswell states that "certain *Echinacea* extracts have shown direct anti-cancer activity in vivo" (column 2, lines 61-64). Facino discloses a method of purifying *Echinacea angustifolia* to obtain a chloroform fraction that has anti-hyaluronidase activity at a certain concentration and acidity (p.1450-1452). Intellisano discloses a food supplement that contains *Echinacea* for an antioxidant and suggests that *Echinacea angustifolia* and *Echinacea purpurea* are interchangeable.

I. A *Prima Facie* Case Of Obviousness Has Not Been Properly Established.

Examiner argues that Applicants are treating cancer and, as such, it is well within the skill of the artisan to carry out the claimed method. However, Applicants respectfully submit that Examiner has not established a proper *prima facie* case of obviousness because Braswell, Facino, and Intellisano are not properly combinable as there is no reasonable expectation of success in substituting Facino's *Echinacea angustifolia* for

Intellisano's *Echinacea purpurea*. Further, this combination does not teach or suggest all the claim limitations, namely, inducing phase II enzymes. MPEP §2142 states that to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. MPEP §2142.

A *prima facie* case has not been properly established because there is no reasonable expectation of success to interchange Facino's *Echinacea angustifolia* for Intellisano's *Echinacea purpurea* and obtain the same results in all applications. The concentration of actives responsible for *Echinacea*'s beneficial effects vary from species to species. It is known by one of ordinary skill in the art that a chloroform fraction from any *Echinacea* species, at any acidity, and at any concentration would not necessarily achieve the same levels of phase II activity and anti-hyaluronidase activity as suggested by Examiner. In fact, the data in support of anti-hyaluronidase activity in Facino and the data in support of Applicant's phase II activity demonstrate that different results can be achieved with different materials and concentrations. See arguments in Section II herein. Because several variables can alter the ability of *Echinacea* to induce phase II enzymes, there is no reasonable expectation of success. The combination of the prior art make it, at best, obvious to try the claimed method but do not make the claimed method for inducing

phase II with chloroform fractions of *Echinacea purpurea* obvious without hindsight reconstruction. Obvious to try is not a sufficient basis for a prima facie case.

Additionally, a *prima facie* case has not been properly established because all the claimed limitations are not met. See MPEP §2143.03. None of the cited references teach or suggest the specific method of inducing phase II by administering lipid soluble chloroform fractions of *Echinacea purpurea*. Because none of the cited references teach or suggest the claimed method for inducing phase II enzymes, the rejection under §103 is improper and this rejection should be withdrawn.

II. Applicant's Method Provides Surprising Results.

Even if the references are properly combined, Applicants believe that the claimed invention is not obvious over the cited art because Applicant's invention provides surprising results as outlined throughout the present specification. MPEP §2144.09 states that, "A prima facie case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." Applicants have found that the lipid-soluble chloroform portion of *Echinacea purpurea* performs surprisingly better than other *Echinacea purpurea* fractions in inducing phase II activity. The phase II inducing activity of the lipid-soluble chloroform portion is greater than one would expect given the prior art teachings. A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness...of the claims at issue. See MPEP §716.02(a) and In re Corkill, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). In the present case, the chloroform fraction (at a neutral pH) of Facino's *angustifolia* shows inferior hyaluronidase inhibition when compared with the ethylacetate fraction (page 1451, paragraph 4 and page 1452, Fig. 1).

As such, if one assumed that *purpurea* and *angustifolia* were interchangeable and affected hyaluronidase inhibition and phase II enzyme induction equally (as suggested by Examiner), one would expect that the chloroform fraction of Applicant's *Echinacea purpurea* would be inferior to the ethylacetate fraction. In contrast, Applicant's chloroform fraction provides surprisingly superior phase II induction results than the ethylacetate fraction as shown in Fig. 2 of the present application. Moreover, Applicant's claimed method provides surprising results because the level of enzyme activity in the root chloroform fraction was 35% higher than the root methanol fraction; the aerial chloroform fraction was 87% higher than the more polar methanol fraction (see p.5, lines 15-20). At 0.09mg/ml of *purpurea* extract, the chloroform fraction from the root portion had 1.86 times the quinone reductase activity of the untreated control (page 9, lines 26-28). Therefore, Applicants believe that the claimed method of inducing phase II enzyme by administering a chloroform fraction of *Echinacea purpurea* is not obvious and is patentable over the prior art.

Acidic
chloroform
extract
for roots
was lower
than
methanol.

III. Conclusion

Applicants have made an earnest effort to place their application in proper form and to distinguish their invention as presently claimed from the cited prior art. Therefore, Applicants respectfully request entry of the amendments and allowance of the pending claims. Alternatively, Applicants request entry of the amendments presented herein in order to place the claim in better form for appeal, notice of which is being concurrently submitted herewith. It is also respectfully requested that the Examiner expeditiously notify the undersigned attorney as to the disposition of the arguments presented herein in accordance with MPEP §714.13.

Respectfully submitted,

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